

P. 4509

VARIATION IN IMMUNITY RESPONSE OF DIFFERENT ANIMALS.

A. T. GLENNY.

Wellcome Physiological Research Laboratories, Beckenham, Kent.

The object of this paper is to record the variation in response shown by individual animals to the same stimulus and to emphasise the necessity in immunological work of using a reasonable number of animals before making any generalisations.

Immunity index. Into each of 52 guinea-pigs 5 c.c. of a diphtheria toxoid preparation were injected. These animals were tested by the Schick test on various days. Of the 52 animals, 3 were negative on the 12th day, 13 on the 14th, 6 on the 16th and so on, while 6 were not immune until the 20th day or later. In addition to the variations among individual animals, group variations can also be found. All 6 guinea-pigs injected on certain of the days chosen became immune in a shorter time than any of another group of 6 injected on a different day. Groups of 6 guinea-pigs were large enough to distinguish between the immunity response produced by the subcutaneous, intraperitoneal and intramuscular injections of toxoid given diluted or undiluted. Had each method been tested on one guinea-pig only, fallacious results might have been obtained. Diphtheria toxoid was given in a dose of 0.2 c.c., either undiluted or diluted with normal saline to 5 c.c. The subcutaneous injection of diluted toxoid or the intraperitoneal injection of diluted or undiluted toxoid was definitely more effective than the subcutaneous injection or intracutaneous injection of undiluted toxoid alone, or the intramuscular injection of the same volume of toxoid undiluted or diluted. Certain individual variations could have been lessened by careful choice of animals, because the failure of certain guinea-pigs in each group could be correlated to a certain extent with the initial poor condition of the animal.

Four guinea-pigs were injected with a Schick dose of diphtheria toxin, and three weeks later a series of weekly Schick tests was commenced. The four animals became negative in 16, 31, 39 and 52 weeks. Different normal guinea-pigs injected intracutaneously each week with Schick toxin gave the first negative response in 20, 22, 25, 31 and 44 weeks, while one guinea-pig died still Schick positive after 32 weekly tests, and one similar guinea-pig did not become negative after 101 weekly tests.

Old guinea-pigs become immune much more rapidly than young ones. Thus four guinea-pigs weighing between 250 and 300 grams became immune, after weekly Schick doses, in 20, 22, 25 and 31 weeks, whereas animals weighing from 800 to 1000 grams became immune in 9, 10, 13, 13, 13 and 18 weeks.

Antitoxin production. Four rabbits of approximately the same weight received the same injection of diphtheria toxoid, followed by another similar injection some weeks later. Three of the rabbits produced no antitoxin as a result of the first injection and two of them none following the second injection, while one animal produced 0.06 units of antitoxin per c.c. of blood within 14 days of the first injection, and 3.5 units following the second injection.

Different horses receiving the same diphtheria toxin produced different concentrations of antitoxin. Thus on good toxin, five horses, which had a natural content of antitoxin before starting injections of between 0.01 and 0.1 unit of antitoxin, produced antitoxin ranging from 400 to 1000 units per c.c., the average being 550; nine horses possessing a natural antitoxin concentration

PROCEEDINGS OF THE PATHOLOGICAL SOCIETY

of 0·1 or more antitoxin per c.c. of blood produced antitoxin varying from 250 and 275 for two horses, up to 1000, 1100, 1400 for three other horses. Similar variations were recorded for small groups of horses injected with weak toxin during a period when good toxin was not available.

Variations in Ramon test value and its relation to the Ehrlich unit value. Horse A over a period of two months gave the following relation between the values of its various bleedings, determined by both the Ramon method and the *in vivo* method, 1, 0·9, 1, 0·9. The ratio of the values could therefore be taken as practically unity and in this case whether one determined the value of the serum by Ramon test or by the guinea-pig method one obtained the same value for the serum. For horse B, the *in vivo* value was always higher than the Ramon value, the ratios on various dates being 2·1, 2, 2, 1·6, 1·5. For horse C the ratios were 0·5, 0·8 and 0·9 giving an average of about 0·7 on the various dates. For horse D the values of various bleedings were determined over a period of five months. The *in vivo* value was always higher than the Ramon value, the ratios running from 2 to 3·3, the average of 10 bleedings being 2·5. It is clear from this record that one could make no general statement regarding the relation of the *in vivo* to the *in vitro* values of antitoxin in horses. It is not suggested that one cannot draw reliable conclusions from such experiments, for one can do so with sufficient accuracy to predict the average that will be given by a series of tests to be performed; our object is to emphasise the risk involved in drawing general conclusions founded on a small number of experiments.

